PENDING CLAIMS IN STK-1 DIV3
(USSN 09/287,500)

69. (Three Times Amended) A method for inducing local tissue formation from a progenitor cell in a mammal comprising the step of implanting in the mammal a morphogenic device at a locus accessible to at least one progenitor cell of the mammal, whereby the morphogenic device induces local tissue formation from the progenitor cell in the mammal, the morphogenic device comprising:

a) an implantable biocompatible carrier,

b) a morphogenic protein disposed in the carrier, the morphogenic protein capable of inducing tissue formation when accessible to a progenitor cell, and

c) a morphogenic protein stimulatory factor (MPSF) selected from the group consisting of IGF-I, hydrocortisone, insulin and parathyroid hormone, wherein said MPSF is disposed in the carrier, and wherein said MPSF is at a concentration effective to synergistically stimulate the ability of the morphogenic protein to induce tissue formation from the progenitor cell.

70. The method according to claim 69, wherein the locus is a jaw bone for use in periodontal or dental reconstructive procedures.

71. (Amended) The method according to claim 69, wherein the locus is a bone defect selected from the group consisting of a fracture, a non-union fracture, a fusion and a bony void.

72. The method according to claim 69, wherein the locus is a joint for use in cartilage and soft tissue repair.

73. The method according to claim 69, wherein the locus is nervous system-associated tissue for use in neural regeneration and repair.

74. (Three Times Amended) A method of accelerating allograft repair and incorporation in a mammal, comprising the step of implanting at a locus in need of replacement bone a matrix-comprising device, whereby the device accelerates allograft repair and incorporation in the mammal, the device comprising:

a) an implantable biocompatible carrier,

b) a morphogenic protein disposed in the carrier, the morphogenic protein capable of inducing tissue formation when accessible to a progenitor cell, and

c) a morphogenic protein stimulatory factor (MPSF) selected from the group consisting of IGF-I, hydrocortisone, insulin and parathyroid hormone, wherein said MPSF is disposed in the carrier, and wherein said MPSF is at a concentration effective to synergistically stimulate the ability of the morphogenic protein to induce tissue formation from the progenitor cell.

75. The method according to claim 74, wherein the matrix of the device comprises allogenic bone.

76. (Three Times Amended) A method of promoting <u>in vivo</u> integration into a target tissue of a mammal an implantable prosthetic device, the method comprising the steps of:

a) providing on a surface of the prosthetic device an osteogenic composition, and

b) implanting the device in a mammal at a locus where the target tissue and the surface of the prosthetic device are maintained at least partially in contact for a time sufficient to permit enhanced tissue growth between the target tissue and the device,

wherein the osteogenic composition comprises (1) an morphogenic protein capable of inducing tissue formation when accessible to a progenitor cell, and (2) a morphogenic protein stimulatory factor (MPSF) selected from the group consisting of IGF-I, hydrocortisone, insulin and parathyroid hormone, wherein said MPSF is at a concentration effective to synergistically stimulate the ability of the morphogenic protein to induce tissue formation from the progenitor cell, and wherein said morphogenic

protein and MPSF are disposed on the surface region in an amount sufficient to promote from a progenitor cell enhanced tissue growth between the target tissue and the device.

77. (Three Times Amended) A method of treating a tissue degenerative condition in a mammal comprising the step of administering a pharmaceutical composition to the mammal, whereby the composition treats the tissue degenerative condition in the mammal, the composition comprising:

a) a morphogenic protein capable of inducing tissue formation when accessible to a progenitor cell in the mammal;

b) a morphogenic protein stimulatory factor (MPSF) selected from the group consisting of IGF-I, hydrocortisone, insulin and parathyroid hormone, wherein said MPSF is at a concentration effective to synergistically stimulate the ability of the morphogenic protein to induce tissue formation from the progenitor cell; and

c) a pharmaceutically acceptable carrier.

78. The method according to claim 77, wherein the morphogenic protein comprises a pair of subunits disulfide bonded to produce a dimeric species and wherein at least one of the subunits comprises a polypeptide belonging to the BMP protein family.

79. The method according to claim 77, wherein the morphogenic protein is an osteogenic protein.

80. The method according to claim 79, wherein the osteogenic protein is capable of inducing the progenitor cell to form endochondral or intramembranous bone.

81. The method according to claim 79, wherein the osteogenic protein is capable of inducing the progenitor cell to form cartilage.

82. The method according to claim 77, wherein the morphogenic protein is capable of inducing the progenitor cell to form tissue tendon/ligament-like or neural-like tissue.

83. The method according to claim 77, wherein the morphogenic protein comprises a polypeptide selected from the group consisting of: BMP-2, BMP-4, BMP-5, BMP-6, BMP-7 (OP-1), BMP-8, BMP-9, BMP-10, BMP-11, BMP-12, and BMP-13, COP-5, COP-7.

84. The method according to claim 77, wherein the morphogenic protein comprises a polypeptide selected from the group consisting of OP-1, BMP-2, BMP-4 and BMP-6.

85. The method according to claim 77, wherein the morphogenic protein comprises OP-1.

86. (Amended) The method according to claim 78, wherein the dimeric species is a homo- or hetero-dimer comprising at least one BMP-2 or OP-1 (BMP-7) subunit.

87. (Amended) The method according to claim 77, wherein the morphogenic protein stimulatory factor is IGF-I.

88. The method according to claim 77, wherein the morphogenic protein stimulatory factor comprises an agent that increases IGF-I bioactivity in the mammal.

90. (Amended) The method according to claim 77, wherein the morphogenic protein is present in the pharmaceutical composition at a concentration of at least about 1 ng/ml, and the morphogenic protein stimulatory factor is present in the pharmaceutical composition at a concentration of at least about 0.01 ng/ml.

91. (Amended) The method according to claim 77, wherein the morphogenic protein is OP-1 and is present in the pharmaceutical composition at a concentration of from about 1 ng/ml to about 500 ng/ml and the morphogenic protein stimulatory factor is IGF-I and is present in the pharmaceutical composition at a concentration of from about 0.1 ng/ml to about 50 ng/ml.

95. (Amended) The method according to claim 77, wherein the morphogenic protein is OP-1 and is present in the pharmaceutical composition at a concentration of from about 1 ng/ml to about 500 ng/ml and the morphogenic protein stimulatory factor is hydrocortisone and is present in the pharmaceutical composition at a concentration of from about 0.05 nM to about 5.0 nM.

96. The method according to claim 95, wherein OP-1 is about 200 ng/ml and hydrocortisone is about 0.5 - 5.0 nM .

97. (Amended) The method according to claim 77, wherein the morphogenic protein is OP-1 and is present in the pharmaceutical composition at a concentration of from about 1 ng/ml to about 500 ng/ml and the morphogenic protein stimulatory factor is insulin and is present in the pharmaceutical composition at a concentration of from about 0.01 nM to about 1000 nM.

98. (Amended) The method according to claim 77, wherein the morphogenic protein is OP-1 and is present in the pharmaceutical composition at a concentration of from about 1 ng/ml to about 500 ng/ml and the morphogenic protein stimulatory factor is parathyroid hormone and is present in the pharmaceutical composition at a concentration of from about 10 nM to about 1000 nM.

99. The method according to claim 98, wherein OP-1 is about 200 ng/ml and parathyroid hormone is about 25-200 nM.

102. The method according to claim 69, wherein the carrier comprises

heparin or a salt thereof.

103. The method according to claim 74, wherein the carrier comprises heparin or a salt thereof.

104. The method according to claim 76, wherein the osteogenic composition further comprises heparin or a salt thereof.

105. The method according to claim 77, wherein the carrier comprises heparin or a salt thereof.